

WHAT IS CLAIMED IS:

1. An isolated human nuclear receptor that binds to a cytochrome P-450 monooxygenase promoter, or a DNA binding or ligand binding domain thereof.

2. The receptor according to claim 1 wherein the promoter is a cytochrome P-450 monooxygenase 3A4 (CYP3A4) promoter.

3. The receptor according to claim 2 wherein said receptor is hPXR.

a 4. An isolated human nuclear receptor having the amino acid sequence given ^{in SEQ ID VS. 14} Figure 1, or a fragment thereof, of at least 30 consecutive amino acids.

5. A fusion protein comprising a DNA binding or ligand binding domain of hPXR and a non-hPXR-derived sequence.

6. An isolated nucleic acid comprising a sequence encoding the receptor of claim 1 or 4 or the fusion protein of claim 5.

7. A construct comprising the nucleic acid of claim 6 and a vector.

8. A host cell comprising the construct of claim 7.

9. A method of making the receptor of claim 3, or fragment thereof, comprising:

culturing a host cell containing an expression construct comprising a sequence encoding said receptor, or fragment thereof, operably linked to a promoter, under conditions such that said receptor, or fragment thereof, is produced, and

isolating said receptor, or fragment thereof.

10. A method of screening a test compound for its ability to induce CYP3A4 gene expression comprising

i) contacting said test compound with the ligand binding domain of hPXR,

ii) determining whether said test compound binds to said ligand binding domain, wherein binding of the test compound to said ligand binding domain is indicative of a compound that induces CYP3A4 gene expression.

11. A method of screening a test compound for its ability to activate or inhibit hPXR comprising:

i) preparing an expression vector comprising a sequence encoding a DNA binding domain and a hPXR ligand binding domain;

ii) preparing a reporter construct comprising a DNA binding site recognized by said DNA binding domain operably linked to a reporter gene,

iii) introducing said expression vector and said reporter construct into compatible host cells,

iv) incubating said cells resulting from step (iii) with said test compound, and

v) determining the level of expression of said reporter gene,

wherein enhancement of expression of said reporter gene in the presence of said test compound indicates that said test compound can activate hPXR, and

wherein inhibition of expression of said reporter gene in the presence of said test compound indicates that said test compound can inhibit hPXR.

12. A compound that induces CYP3A4 identified by the method of claim 10.

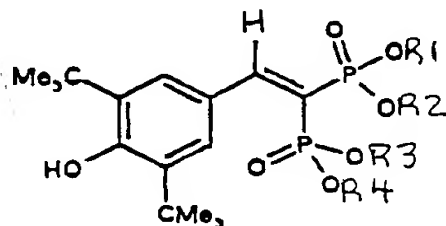
13. A compound that activates hPXR identified by the method of claim 11.

14. A method of modulating function of a cell mediated by PXR comprising contacting said cell with a compound identified using the method of claim 11 that activates PXR under conditions such that said activation is effected and said function is thereby modulated.

15. A method of modulating function of a cell mediated by PXR comprising contacting said cell with a compound identified using the method of claim 11 that inhibits PXR under conditions such that said inhibition is

effected and said function is thereby modulated.

16. The method according to claim 14 or 15 wherein said compound is of formula I:



wherein R₁, R₂, R₃ and R₄ are, independently, C₁-C₈alkyl, linear or branched.

17. The method according to claim 14 or 15 wherein said cell is a cultured cell.

18. The method according to claim 14 or 15 wherein said cell is present in a tissue.

19. The method according to claim 14 or 15 wherein said cell is present in an animal.

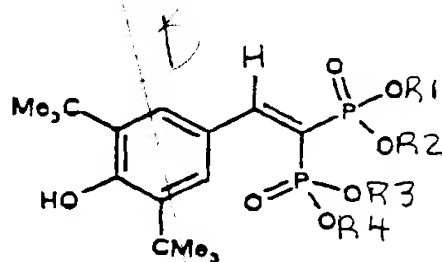
20. A method for associating a particular disease or condition with modulation of PXR comprising

contacting a compound that binds to PXR specifically with PXR present in a cell under conditions such that said binding is effected

and a functional activity of said cell mediated by PXR is thereby modulated,

detecting said modulation of said functional activity and associating said modulation of said functional activity with a disease or condition and thereby associating said disease or condition with modulation of PXR.

21. The method according to claim 20 wherein said compound is of formula I:



wherein R₁, R₂, R₃ and R₄ are, independently, C₁-C₈alkyl, linear or branched.

22. The method according to claim 21 wherein said compound is GW-485801.

23. A method of preventing or treating a disease or condition that has been associated with modulation PXR by the method of claim 20, comprising administering to a patient in need thereof a therapeutically effective amount of an agent that modulates the activity of PXR so that said prevention or treatment is effected.

24. The method according to claim 23
wherein said agent is GW-485801.

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